MEDICAL PRACTICE

Contemporary Themes

Ablative radioiodine therapy for hyperthyroidism: long term follow up study

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Abstract

A total of 225 patients were treated for hyperthyroidism with 555 MBq (15 mCi) radioiodine to ablate the thyroid and induce early hypothyroidism. The efficacy of this treatment in eradicating hyperthyroidism and problems of follow up were assessed one to six years later from case records and questionnaires. Information was received from 197 out of 219 live patients (90%) and from 160 doctors concerning 207 patients (92%). Only three patients were not traced and six had died since treatment. The modal time to hypothyroidism was three months, and 64% of patients were hypothyroid at one year; 5·6% had failed to become euthyroid within one year. Ninety five per cent of patients had been seen by the doctor and 82% had had a thyroid test done within the past two years. Most doctors preferred patients to be returned to their care once thyroxine treatment was stabilised.

An ablative dose of ^{131}I is recommended as an effective means of treatment which has clear advantages over conventional methods. Good communications and effective follow up should ensure success.

Introduction

Radioiodine therapy is an effective method of treating hyperthyroidism and has the advantages of safety, ease of administration, cheapness, and relative freedom from side effects. The main problems associated with its use are delay in controlling hyperthyroidism and the ensuing high incidence of hypothyroidism. The incidence of hypothyroidism increases with time from treatment,[1-3] and patients may become hypothyroid many years later when they have been lost to follow up. Attempts to reduce the incidence of hypothyroidism have included the use of a lower absorbed radiation dose to the thyroid,[4] but this results in an unacceptable number of patients remaining hyperthyroid, and increasing the accuracy of the dosimetry by taking into account the uptake of ^{131}I in the thyroid and the size of the gland.[5] Plainly an ideal dose that would quickly correct the hyperthyroidism without any risk of subsequent hypothyroidism does not exist. Another approach is to ablate the thyroid with a larger dose of ^{131}I[6] to correct the hyperthyroidism rapidly and induce early hypothyroidism which can then be easily managed by thyroxine replacement treatment under close medical supervision. This approach has not gained widespread acceptance because of uncertainty about frequency of defaulting, frequency of non-compliant patients who later discontinue thyroxine, adequacy of follow up by the general practitioner, or possible complications such as cancer or ischaemic heart disease. A policy of an ablative dose regimen has, however, been in use in this hospital for several years; this study was therefore designed to assess the efficacy of the treatment and follow up.

Methods

Therapeutic regimen—Hyperthyroidism was diagnosed on the basis of clinical and biochemical features. Toxic nodular goitre was differentiated from Graves' disease by radioisotope scintigraphy. Patients received a standard 555 MBq (15 mCi) oral dose of radioiodine regardless of size of the gland or severity of the disease. They were warned beforehand that they would probably become hypothyroid and need lifelong replacement treatment, and they agreed to this. Patients were not given carbimazole but some received propranolol for temporary relief of symptoms. Follow up was at six weeks initially

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and then two monthly either until the patient had become hypothyroid or till the end of one year, after which repeat visits were as considered appropriate by the clinician.

At each visit a clinical assessment was made and samples sent for thyroid tests. The diagnosis of hypothyroidism was confirmed by finding a reduced serum free thyroxine index and a raised thyroid stimulating hormone concentration. Thyroxine treatment was started at the earliest evidence of hypothyroidism and the dose adjusted as appropriate up to the full replacement dose of 0·15 mg daily. When the hypothyroidism was stablised on a replacement dose of 0·15 mg daily, and provided that no complicating factor such as severe eye disease was present, the patients were referred back to their family doctor for long term follow up. At that time patients were told verbally that they should continue thyroxine for the rest of their lives. A letter was sent to the general practitioner to say that thyroxine would need to be continued indefinitely, usually in a dose of 0·15 mg daily, but suggesting that thyroid function tests should be carried out if any intercurrent problems developed. The doctor was also informed that no further hospital appointment had been given. Patients yet to require thyroxine treatment continued to be seen regularly in the hospital clinic.

Data collection—Information was sought regarding compliance of the patient, adequacy of follow up, other medical problems—particularly carcinoma and ischaemic heart disease—which may have occurred since treatment, the doctor's assessment of the follow up scheme, and recommendations for improvement. Patients who had been treated by the endocrine unit with an ablative 555 MBq dose of radioiodine were identified from records held in the radiotherapy department. Questionnaires were sent to all these patients and a separate questionnaire sent to each patient's family doctor; when notification of change of address or change of practitioner was received further questionnaires were sent. When no reply was received a second questionnaire was sent. The hospital case notes of all patients were checked for the date at which hypothyroidism had been diagnosed and thyroxine treatment started and for further details regarding other medical problems.

Results

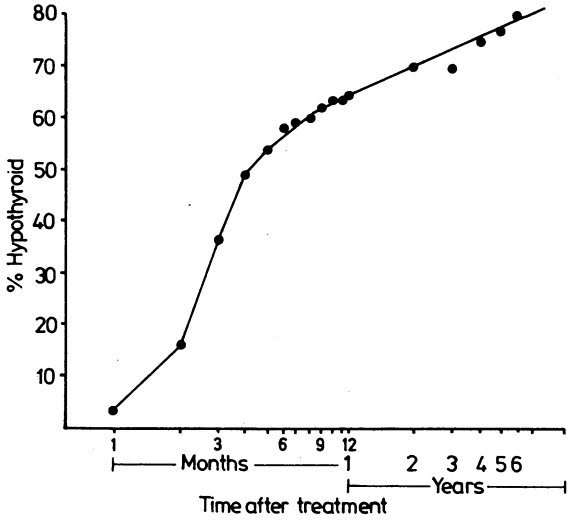
A total of 225 patients were included in the survey. Their mean age at the time of treatment was 55 years (range 21-84); only five were less than 35. Women outnumbered men by 6·3 to one. Eleven patients had toxic nodular goitre and the remainder had Graves' disease. Ten patients (4·4%) required a second dose of 555 MBq ^{131}I since they were still hyperthyroid one year after treatment and three of these required a third dose. In all, 12 patients failed to become euthyroid within one year of treatment. The length of time since treatment was two years or more in 195 patients and five years or more in 111.

Analysis of data—Of the 225 patients surveyed, six had died and 197 replied, giving a patient response rate of 88% (90% of those still living). Replies were received from 160 individual family doctors concerning 207 patients (92%). A few patients for whom no completed questionnaires were available were still attending the hospital clinic, so that necessary data could be obtained from the case notes. The total number of live patients for whom no up to date information was available was three, one of whom had returned to the Middle East with instructions for follow up. Data for 215 patients were analysed, which excluded the six who had died and four for whom there were inadequate data.

Thyroxine replacement treatment—Of the 215 patients analysed, 153 (71·2%) were taking thyroxine. Three of these had been treated for toxic nodular goitre. The modal time from treatment to hypothyroidism for patients who received a single dose of 555 MBq ^{131}I was three months. One hundred and nineteen of these patients (58%) had become hypothyroid by six months and 132 (64%) at one year. The figure shows the distribution of time to hypothyroidism. Replies from the family practitioners indicated that three patients (1·4%) who had begun thyroxine were no longer taking it; of these, one patient claimed that she was taking it and quoted the dose, one had never seen his doctor, and the third patient said that he thought he needed thyroid hormone. Fifty nine patients remained euthyroid—that is, 27% of all patients treated. From the doctors' replies 3% of patients were considered to be non-compliant and 81% compliant; the question was unanswered for the remaining patients. Table I compares non-compliance with time since treatment.

Other medical problems—Information about general medical history after ^{131}I therapy was culled from the general practitioners' replies, patients' replies, and hospital case notes and was obtainable for 220 patients (table II). Twelve patients aged 50-74 years (5·4%) were diagnosed as having ischaemic heart disease, of whom two were men and 10 women; two of these patients had died from myocardial infarction. Seven patients (all women) aged 50-74 had developed carcinoma, of whom three had died; the sites were (one each) breast, colon, endometrium, stomach, lung, thyroid, and myeloma. The patient with thyroid cancer was treated for a very large toxic nodular goitre and died within weeks, indicating that the initial diagnosis was almost certainly carcinoma. Table II lists other conditions that had occurred since treatment. The figure for arthritis was probably inaccurate, since many patients complained of musculoskeletal pains which had no precise diagnosis. Six patients had died since treatment —two from myocardial infarction, three from cancer, and one from unknown cause; table III gives the details.

Medical follow up—Out of a possible 217 patients, 180 (83%) had seen their family doctor within the previous year, but 11 (5%) had not seen their doctor for two years or more. A total of 124 (67%) had had thyroid function values checked within the past year, but 34 (18%) had had no test for at least two years (table I). Family doctors were asked whether they considered that the responsibility for long term follow up of radioiodine treated patients should rest primarily with the hospital or with the family doctor; 118 (74%) replied in favour of the latter. Many of these commented that patients should be transferred back to the general practitioner's care only when they



Incidence of hypothyroidism after single dose of 555 MBq (15 mCi) ^{131}I (n=205).

TABLE I—*Follow up data for patients treated with 555 MBq (15 mCi) ^{131}I. Figures are numbers of patients*

	Years since treatment							Total
	7	6	5	4	3	2	1	
Failing to take thyroxine	0	1	2	0	0	0	0	3
Considered by general practitioner to be non-compliant	2	1	2	1	1	0	0	7
Not seen by general practitioner for >2 years	1	4	0	5	1	2	—	13
No thyroid tests for >2 years	1	12	9	12	0	0	—	34
Untraceable	0	2	1	0	0	0	0	3

TABLE II—*Conditions occurring after ^{131}I therapy (220 patients)*

	No (%) of patients		No (%) of patients
Ischaemic heart disease	12 (5·4)	Acromegaly	2 (0·9)
Hypertension	10 (4·5)	Osteoporosis	2 (0·9)
Arthritis	7 (3·2)	Diabetes mellitus	2 (0·9)
Cancer	7 (3·2)	Chronic obstructive airways disease	2 (0·9)
Psychosis	4 (1·8)	Ulcerative colitis	1 (0·4)
Peptic ulcer	4 (1·8)	Polymyalgia rheumatica	1 (0·4)
Pernicious anaemia	3 (1·4)	Pancreatitis	1 (0·4)
Glaucoma	3 (1·4)	Paget's disease	1 (0·4)
Addison's disease	2 (0·9)		

TABLE III—*Details of deaths after 555 MBq (15 mCi) ^{131}I*

Case No	Sex	Age at death (years)	Time since ^{131}I	Diagnosis
1	F	59	5 years	Gastric carcinoma
2	F	55	2 years	Carcinoma of lung
3	F	66	2 months	Thyroid carcinoma
4	M	70	5 years	Myocardial infarction
5	F	66	5 years	Myocardial infarction
6	F	59	5 years	Unknown

had become hypothyroid and were stabilised on thyroxine replacement treatment. Many helpful points were made, with emphasis on (*a*) the need for good communication between hospital and patient and with the family doctor, and (*b*) the need of the family doctor for a follow up system with an effective means of recall for non-attenders. More specifically, information for the doctor's use was requested concerning recommended follow up after discharge from the hospital clinic and also for some printed instructions to patients in addition to the usual verbal explanation.

Discussion

An ablative dose of ^{131}I is effective in eradicating hyperthyroidism. Most patients rapidly become euthyroid or hypothyroid. Antithyroid drugs were needed in only 12 patients and a repeat dose of ^{131}I was required in 10 (4·4%). This is much more satisfactory than the response seen after conventional treatment and confirms the finding of Wise *et al.*[6] It is well established that the rate of hypothyroidism is dose dependent[4]; as expected, a high proportion of patients in this study developed hypothyroidism, 156 (73%) of all the patients requiring thyroxine at the time of the survey. This contrasts with conventional doses, where the rate of increase of hypothyroidism after the first year is roughly 3% a year, so that at five years after treatment the incidence of hypothyroidism is about 30%,[1] at 10 years 40-70%,[1 2] and at 15 years 50-80%.[2 3] Clearly the insidious onset of hypothyroidism so long after treatment of the hyperthyroidism is much more likely to be missed than when hypothyroidism is deliberately induced under medical supervision. If the use of an ablative dose of ^{131}I is adopted it is mandatory that everything possible should be done to ensure that patients continue with lifelong thyroid replacement. The default rate—that is, those lost to follow up and those who discontinued thyroxine—was in fact well below that of a follow up study of patients treated with conventional dosage[7]; ways in which our follow up might be improved have been identified and their implementation should certainly lower the default rate still further.

It is well established that a conventional dose of 70 Gy (7000 rads) ^{131}I to the thyroid is not carcinogenic,[8 9] and may even be protective. There is no reason to suppose that the 555 MBq (15 mCi) dose would be carcinogenic, and the seven cases of cancer noted in the 50-74 year age group (4·3% of patients in this age group) are no more than would be expected in the general population. Hypothyroidism may predispose to ischaemic heart disease, and this is sometimes quoted as an anxiety with this form of ablative treatment; nevertheless, 12 patients in the 50-74 year age range (7·5% of patients in this age group) again does not represent an increase over the expected number.

As a result of this study we recommend a policy of an ablative dose of ^{131}I for hyperthyroidism. The follow up programme that we intend to adopt is as follows: (*a*) all patients will be followed up in the endocrine clinic at frequent intervals until hypothyroid, and steps will be taken to ensure that these patients are not mistakenly discharged until they have been stabilised on thyroxine; (*b*) when a patient is stable on thyroxine 0·15 mg daily she or he will be given a card stating the lifelong requirement for thyroxine treatment and advising a yearly check up with the general practitioner; (*c*) a standard letter will be sent to the general practitioner advising him that the patient has been discharged from the clinic, should continue lifelong thyroxine, and should have a yearly check up with measurements of serum thyroxine; (*d*) we intend to enter data concerning patients treated with ^{131}I into a computer register to facilitate follow up and to update the records at two year intervals with the help of the general practitioner. We consider that the exercise reported here has been worth while because, firstly, it has established that an ablative dose regimen is satisfactory treatment; secondly, it has enabled us to improve our practice; and, thirdly, we have identified and now treated some patients who had escaped follow up.

We are grateful to all the doctors who replied to our questionnaire for their very helpful comments.

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(*Accepted 17 May 1984*)

What are the hazards of using intrauterine contraceptive devices?

Women who use intrauterine devices are more likely to develop pelvic inflammatory disease than women who do not. The risk of acute infection is greatest within the first 12 months of use, and thereafter tends to decline progressively.[1] The uterine cavity is normally sterile and organisms may be introduced at the insertion of the intrauterine device through the constantly contaminated cervix, but the uterus normally sterilises itself within 30 days.[2] Organisms may persist and maintain the potential to produce pelvic inflammatory disease at a later date.[3] This may in part account for its high incidence in the first year, and more frequent insertions would tend to increase the risk of infection. Later colonisation may also occur and the intrauterine device thread and coital factors have been causally implicated, but there is no sound clinical evidence that more frequent changing of the device would reduce infection from this source. Colonisation by actinomyces like organisms occurs with long term use, particularly with inert devices, but actinomyces is a rare cause of pelvic inflammatory disease in women with intrauterine devices. It has been suggested that copper in the endometrial fluid may inhibit the ascent of gonococci. If this does have a protective function it is unlikely that the risk of gonococcal infection would be further reduced by the early reinsertion of copper devices before the end of the recommended active period. The optimal duration of use for inert devices remains uncertain, but the evidence suggests that they may safely remain in utero for many years. Copper bearing devices, on the other hand, should be changed at the recommended period to maintain effective contraception. To minimise infective complications associated with intrauterine devices women must be carefully counselled and encouraged to report gynaecological symptoms. Routine medical examination is advised, particularly for long term users.—P M FISHER, consultant obstetrician and gynaecologist, Aberdeen.

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